

Eminent Indians in Medicine

Dr P.K. Rajagopalan



Dr Pylore Krishnaier Rajagopalan is a biologist best known for his work on vector control in India and his research on Kyasanur forest disease. He was born in Mukteshwar, Uttarakhand and graduated from the Banaras Hindu University in 1949 and completed his masters in Zoology in 1951. In 1952, he joined the Virus Research Centre, Pune. Later, he was awarded a fellowship by the Rockefeller Foundation, USA, to pursue a Master's in Public Health in University of California, Berkley. On his return to India in 1960, he joined the Institute of Virology where he was given the responsibility of leading the investigation of KFD, a disease which was recorded for the first time in 1957. He founded the Vector Control Research Centre in 1975 in Puducherry, where he started the first MSc course in Medical Entomology in India. Besides KFD, he has worked on various vector-borne diseases such as Japanese encephalitis, malaria and filaria. He was awarded the Padma Shri by the Government of India in 1990 and has been felicitated with various other awards such as P.N. Raju oration award of the Indian Council of Medical Research in 1980, Om Prakash Bhasin Award for Science and Technology in 1985 and Charles University, Prague, Gold Medal in 1988. He is an elected Fellow of the Royal Society of Biology and the Royal Society of Tropical Medicine.

The first outbreak of Kyasanur forest disease (KFD) occurred in 1957 in Shimoga (now Shivamogga) district of Karnataka. Since then, many epidemics of KFD have occurred in different parts of the Western Ghats. The latest epidemic occurred in Aralagodu, Karnataka, where the first suspected case of KFD was reported on 24 November 2018. Between November 2018 and April 2019, a total of 342 people were affected and 12 died due to KFD in Shimoga. November to May is usually labelled as the KFD season. Vaccination has not proven to be effective in its prevention and the treatment continues to be hospitalization and supportive care.

In the following exclusive email interview, Dr P.K. Rajagopalan, the person who has been credited with pioneering work in the field of KFD and other vector-borne diseases, shared his experiences on KFD and related research. Dr Rajagopalan stays in Chennai, Tamil Nadu.

NMJI: How was KFD discovered first?

Dr Rajagopalan: KFD was an accidental discovery. When an episode of human and monkey deaths was reported from the forests near Sagar, Shimoga district, it was thought that yellow fever (YF), which was eluding India, had broken out. On investigations, it was found to be a tick-transmitted haemorrhagic disease, closely related to Omsk haemorrhagic fever, belonging to the Russian Spring Summer Encephalitis (RSSE) group of viruses.

NMJI: In which place was it exactly discovered in Shimoga?

Dr Rajagopalan: The first isolation was from the tissues of a dead monkey collected from Kyasanur forest, near Barige village, in Sagartaluk, and hence named KFD.

NMJI: Since Jorge Boshell-Manrique's initial publication of isolation of the virus causing KFD in 1968, how far has the journey of KFD moved?

Dr Rajagopalan: All our studies led to the conclusion that the disease was there in many pockets in a silent enzootic form, and due to the changes in the biocoenotic relationships caused by human interference with nature. In this case, it was the construction of Sharavathy Hydroelectric Dam. The seed virus is already almost everywhere in the forest range. There is no question of KFD moving from place to place. Wherever it raises its head, you come to know of it.

NMJI: I learnt from a couple of articles that he was your mentor, 'guru'. What kind of person was he? On which projects did you collaborate with him?

Dr Rajagopalan: Boshell was in the KFD area for 5 years, as the chief investigator, and I was his deputy. He was a remarkable individual, highly knowledgeable in arboviruses, forest ecology and above all a good human being. Everyday, we would visit the forests together, and he used to tell me his experience in other

parts of the world. I almost started worshipping him for his knowledge. I learnt a lot from him.

NMJI: How does KFD spread?

Dr Rajagopalan: KFD spreads from one area to another, wherever the virus-carrying monkeys move and drop the fed larvae of *Haemaphysalis*, and when they moult into nymphs carrying the virus, they transmit to new hosts. It is a complicated process involving monkeys, who have their own territories. Monkeys do not move far away carrying infected ticks into new areas. That will be another foci, where another silent enzootic with small mammals may be occurring.

NMJI: Why is the Western Ghats area more prone to this disease? Is KFD or similar diseases found in other areas of the world? Why has KFD spread out from Shimoga to other places in the Western Ghats?

Dr Rajagopalan: The Western Ghats have a typical ecosystem of both moist deciduous and tropical evergreen forests, but KFD has sprouted out mostly from moist deciduous forests.

NMJI: Initially KFD was thought to be yellow fever; how were the two distinguished?

Dr Rajagopalan: Antigenically, these are two different viruses. Initially, KFD was thought to be YF, because in both YF and KFD, humans and monkeys are affected.

NMJI: Is there any hypothesis on the possible route by which the virus escapes the bat–tick–bat cycle to enter small mammals?

Dr Rajagopalan: This is the most important aspect which has to be investigated. It needs dedicated scientists such as the team of the Rockefeller Foundation, with unlimited funds to go deep into the forests and look for evidence, without waiting for quick results for publishing a paper. There is little hope from the present generation.

NMJI: Could you briefly explain how does KFD transmission occur? Which are the agents involved in its transmission?

Dr Rajagopalan: It is simple. KFD transmission occurs only through the bite by an infected questing nymphal stage of an infected tick. There is no aerosol transmission.

NMJI: Which tick species are involved in KFD? Which of them is most significant in the transmission to human beings?

Dr Rajagopalan: Mostly *Haemaphysalis spinigera*, *H. turturis* and *H. papuanakinneari*. Though the virus has been isolated occasionally from other species, they have no role in the transmission of disease.

NMJI: What is the role of monkeys in the transmission of this disease? What causes their death after they are infected by the virus?

Dr Rajagopalan: They are amplifiers of the virus. They may get infected by one single nymph; but they transmit the infection to hundreds of larvae, which when they are dropped along with the travelling monkey, become foci for infection. Monkeys, like humans, suffer from acute haemorrhage, causing death.

NMJI: Why were monkeys from different areas getting affected each time?

Dr Rajagopalan: Every time they have to get bitten by an infected tick, if they are present in that spot. It is a question of chance.

NMJI: What role does climate change play in the transmission of KFD? Which is the season of highest prevalence of KFD?

Dr Rajagopalan: Climate change has an impact on the growth and soil of vegetation, which really impacts on tick density. The season of highest prevalence is the period between two monsoons, when the nymphal population of ticks is maximum.

NMJI: What has been the Rockefeller Foundation's role in unravelling the KFD mystery?

Dr Rajagopalan: The disease would not have been recognized without guidance from the Rockefeller Foundation. They helped in establishing the similarity of infection in both monkeys and humans, common in both YF and KFD. In fact, the then Mysore government declared Sagar epidemic as typhoid and started free distribution of chloromycetin capsules.

NMJI: What are the questions related to KFD that remain unanswered and need further research?

Dr Rajagopalan: Two major investigations are necessary. First, how are the infection chains of bat–ornithodoros–bat cycle and the shrew/small mammal *Haemaphysalis/ixodes* cycle related?

Second, one has to look for *Rhinolophus* bat colonies in many areas deep in the forests to know whether the new foci for transmission could originate there. It is a long-term field study in many areas and has to be coordinated by an organization such as the Rockefeller Foundation. It seems a distant dream at present.

NMJI: Please share your KFD journey with us. How did the mystery of the strange disease unfold over time?

Dr Rajagopalan: It is no longer a mystery. I worked for 13 years living in a village in the forest. I found this a fascinating epidemiological event, something like a detective story, and enjoyed every minute of it, got encouragement and appreciation from the Rockefeller Foundation, and rewards too. After 1970 (when I was transferred to Delhi), nobody has ventured to work in the forests.

NMJI: You once contracted KFD but recovered soon. How was that phase when you were suffering from KFD? The signs, symptoms, course and your final recovery?

Dr Rajagopalan: The clinical symptoms are well documented. In my case there was also the involvement of the central nervous system, and my eye sight was affected. The Rockefeller Foundation spent a lot of money on my treatment and convalescence.

NMJI: What was the role of Salim Ali in attempting to unravel the mystery of KFD? Please elaborate.

Dr Rajagopalan: Since KFD is related to RSSE virus, birds were suspected to have brought the virus/infected ticks. I worked on this subject, collecting nearly 9000 birds over a 2-year period, and Dr Salim Ali was my advisor on birds. He was my guide for my PhD from Pune University.

NMJI: What's 'Boshell's cup of coffee' analogy in KFD?

Dr Rajagopalan: It is a beautiful analogy; just like a good cup of coffee is dependent on many factors, a KFD case can occur only because of several factors (Fig. 1).

NMJI: What is the concept of 'nidality' in KFD?

Dr Rajagopalan: The concept of natural nidality (Pavlovski)



FIG 1. Boshell's cup of coffee analogy in Kyasanur forest disease (KFD) (courtesy Dr P.K.Rajagopalan)

means that wild enzootic foci of many diseases exist in nature independent of humans and domestic animals. These foci present well-defined ecological peculiarities wherein pathogens and natural hosts are associated, often through an intermediate vector. This is true also for KFD.

NMJI: How could KFD have travelled to India? What was its place of origin?

Dr Rajagopalan: KFD is an indigenous virus; it is already in India. It has appeared due to certain environmental and ecological factors.

NMJI: What advancement has been made in prevention and treatment of KFD from 1957 to 2019?

Dr Rajagopalan: None.

NMJI: What has been the role of the Indian Council of Medical Research (ICMR) in KFD?

Dr Rajagopalan: After the withdrawal of the Rockefeller Foundation in 1970, the Virus Research Centre became the National Institute of Virology, and since then it is passive, working mainly on basics.

NMJI: How is the current generation of entomologists continuing the KFD research further? Are they as enthusiastic as you were?

Dr Rajagopalan: They are more interested in molecular entomology, not in fieldwork.

NMJI: You have given a talk in Goa about malaria and the malaria control programmes in India. How successful has the National Malaria Eradication Programme been?

Dr Rajagopalan: The National Malaria Eradication Programme is now called the National Vector Borne Disease Control Programme. It is too much work in a vast country; with each state behaving erratically in following their guidelines, since health is a state subject. They are trying their best.

NMJI: What do you think is the biggest lacuna in the National Malaria Eradication Programme that needs to be addressed?

Dr Rajagopalan: There is a need for more decentralization and to fill up the many vacant posts of entomologists. The country is too

vast for a single organization functioning from Delhi.

NMJI: Have you worked on dengue and chikungunya also? Where does India stand in management of these vector-borne diseases and what needs to be done further in these fields?

Dr Rajagopalan: No.

NMJI: What are the lessons learnt from your life dedicated to vector-borne disease control that you would like to share with the medical fraternity and young researchers?

Dr Rajagopalan: It is the knowledge you get only by working in the field and not in air-conditioned laboratories with computers.

NMJI: What do you see as the biggest roadblock in furthering research in prevention, control and management of vector-borne diseases?

Dr Rajagopalan: There are square pegs in round holes; no vision, a set of so-called experts sitting in judgement, who show progress only by beautiful reports. But everyone makes money. It is all safari research and survival research.

NMJI: What has been your biggest regret (if any) that you wish you could have accomplished but did not?

Dr Rajagopalan: I have no regrets. I got full support and encouragement from the Rockefeller Foundation, then from three of the most distinguished Director Generals of the ICMR. I did a lot of work and achieved global recognition.

NMJI: What are the diagnostic tests used for laboratory confirmation?

Dr Rajagopalan: In my days, there were no readymade kits, which help the present-day researchers to even fudge results. We used Swiss mice, neutralization tests and HAI tests, in tissue culture, etc. They were reliable.

NMJI: Are there any closely related viruses circulating in India which can confound the diagnostic tests?

Dr Rajagopalan: I am not a virologist, basically. Maybe. But not definitely known.

NMJI: Please tell us something about the associated fatality and complications of the illness.

Dr Rajagopalan: If not treated promptly, death is certain in KFD. Hospitalization and supportive treatment are a must.

NMJI: Besides advances in preventive aspects, mostly related to vaccines, what are the other steps for prevention (from getting infected)?

Dr Rajagopalan: KFD has never been reported in humans other than those in a forest ecosystem. It is a forest disease. Only if you get bitten by an infective tick you get the disease. The repellants are not effective. My experiments on tick control on the forest floor along with Dr Robert Drummond, of United States Department of Agriculture, using insecticidal sprays, also proved futile in destroying ticks. Vaccine is not effective due to various reasons including coverage. Therefore, unless an efficient vaccine is available, the only way to prevent an infection is to avoid frequenting the forest, which is a tall order considering that the livelihood of many people depends on the forests!

NMJI: Please tell us something about your childhood, early days at school. How were those days different from now?

Dr Rajagopalan: My childhood was spent in happy, but not affluent, conditions. I studied in a village school in Kerala, which had dedicated teachers. There was strict discipline. We were studious. There is no comparison with the present-day situation.

NMJI: What inspired you to choose vector-transmitted diseases as your field of work?

Dr Rajagopalan: After MSc, I was looking for a job. Any job. The job of a Research Assistant at the Virus Research Centre was my first one. So I stuck to that.

NMJI: Who has been your biggest inspiration?

Dr Rajagopalan: The working method of the Rockefeller Foundation.

NMJI: What is your biggest support system?

Dr Rajagopalan: None.

NMJI: What roles have your parents and your wife played in shaping your career?

Dr Rajagopalan: They never interfered with whatever I wanted to do.

NMJI: Tell us something about your wife, her education, career etc.

Dr Rajagopalan: My wife is a simple woman. We had an arranged marriage. She had studied up to SSLC only and is a housewife. She is with me aged 81 to my 89 years.

NMJI: Who is your favourite shishya who has furthered your studies?

Dr Rajagopalan: My favourite shishya was one Dr M.A. Sreenivasan, who worked with me. He is no more. When I was Director, I had many assistants. Most of them have also retired now. But none of them is working on these subjects. I still work on vector-borne diseases.

NMJI: Which is the fondest memory ever that you would like to share with the readers?

Dr Rajagopalan: While being honest in doing your work, learn to call a spade a spade. People like honesty more than sycophancy. This is the lesson I had learnt.

NMJI: What message would you give to young researchers as they embark on their journeys? What was your formula of your success?

Dr Rajagopalan: Everyone would have to find their own niche in the environment and learn to adjust and survive. There is no specific formula.

Conflicts of interest. None declared

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